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Letter to the Editor

Role of rotavirus vaccination on an emerging G8P[8] rotavirus strain causing an outbreak in central Japan

The manuscript by Hoque et al. reports the role of rotavirus vaccination on the emerging G8P[8] rotavirus A strains that caused a local outbreak in Shizuoka, Japan, during the 2017 rotavirus season [1]. Apart from whether or not a favorable result was due to the sharing of the P[8] VP7 genes between the vaccine strains and the outbreak strains, we welcome their findings, which lend strong assurance to current global recommendations of the use of rotavirus vaccines for the prevention of severe rotavirus gastroenteritis (RVGE) and encourage public health authorities to expedite the introduction of the rotavirus vaccine to infant immunization schedules in countries where the introduction has been delayed, such as Japan.

Regrettably, however, we noticed an apparent methodological inconsistency in the calculation of vaccine effectiveness (VE), which we wish to draw to the authors' attention for clarification. According to the authors, they designed a case-controlled study using rotavirus-negative patients as controls, which itself is being increasingly used and has gained acceptance [2]. This test-negative design aimed to estimate the VE by comparing the frequency of vaccination exposure of RVGE case-patients with the background frequency of control-patients who were free of rotavirus. Testing of all surveillance specimens indicates that these "test-negative controls" have similar healthcare-seeking behaviors for diarrheal illness to cases with confirmed rotavirus [3]. In Fig. 2 and Table 2, however, the authors divided the patients into vaccinated and unvaccinated groups [1], which suggests that they conducted a cohort study similar to those typically used in randomized clinical trials [4]. Moreover, they calculated attack rates of G8P[8] in vaccinated and unvaccinated patients instead of vaccine coverage among case and control patients.

According to the values and categorization of patients described in Fig. 2 and Table 2 [1], we understand that there were 41 G8P[8] -RVGE cases of which 22 were vaccinated and 19 were unvaccinated, and 20 test-negative controls of which 14 were vaccinated and 6 were unvaccinated. Therefore, a simple chi-squared test produces a crude odds ratio of 0.50 with lower and upper limits of the 95% confidence interval (CI) of 0.16 and 1.55. This indicates that the estimated VE against RVGE by emerging G8P[8] strains was 50% (95%CI: −55% to 84%). The small sample size and low statistical power (23%) would have made it difficult to detect statistical significance for a VE of 50% against G8P[8] -RVGE. When stratified by severity of RVGE, the authors estimated a VE by using G8P[8] -RVGE cases only, without including test-negative controls. Therefore, in the strict sense of the term, what the authors calculated does not represent the VE.

While the issues raised here do not change the overall results of the study, the methodological inappropriateness, if present as we suspect, needs to be clarified. Moreover, despite the methodological inconsistencies, we share the authors' view that currently-licensed vaccines play a pivotal role in preventing children from developing severe disease, including those with G8P[8] -RVGE.

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